

25. (Twice Amended) A method of screening a candidate compound *in vitro* for susceptibility to *in vivo* biliary excretion by an endogenous sinusoidal or canalicular transport system, or by both sinusoidal and canalicular transport systems, the method comprising the steps of:

- (a) providing a culture of hepatocytes, the culture comprising at least one bile canaliculus;
- (b) simultaneously exposing a candidate compound and a pre-selected amount of a marker compound that is a substrate for an endogenous sinusoidal or canalicular transport system, or for both sinusoidal and canalicular transport systems to the culture for a time sufficient to allow uptake;
- (c) washing the culture; and
- (d) detecting an amount of marker compound present in the at least one bile canaliculus in the culture to evaluate uptake and excretion competition between the candidate compound and the marker compound, the presence or the absence of a reduced amount of the marker compound as compared to the pre-selected amount of marker compound indicating the susceptibility of the candidate compound to biliary excretion by an endogenous sinusoidal or canalicular transport system, or by both sinusoidal and canalicular transport systems.

#### REMARKS

##### Status Summary

The United States Patent and Trademark Office (hereinafter the "Patent Office") has examined claims 1-11, 13-23, and 25-64, as presented in the present U.S. patent application, which was filed on March 17, 2000, and new claims 65-66, which were presented in Amendment A submitted on September 17, 2000. It noted that claims 12 and 24 were canceled in the previously submitted Amendment A; but it appears that reference to these claims was inadvertently